SOME PHYSIOLOGICAL EFFECTS OF ACETYLSALICYLIC ACID AND SODIUM SALICYLATE IN THE CHICKEN

BRUCE GLICK

Mississippi Agricultural Experiment Station, State College, Mississippi

According to Krantz et al. (1946) the growth rate of rats was not affected after receiving 0.50 percent acetylsalicylic acid for eight wk. On the other hand, 20 gr of acetylsalicylic acid appeared to increase weight in the dog, (Gaebler et al., 1957). Salicylate stimulates the rat adrenal cortex, apparently by releasing ACTH, (Cronheim et al., 1952) (Barnett and Teague, 1958). Field (1945) and Clark and Spitalny (1946) reported that acetylsalicylic acid had a hypoprothrombinemic effect in rats. A review of the literature concerning the effects of the salicylates in mammals can be found in the monograph by Gross and Greenberg (1948).

The purpose of this paper is to report observations concerning the effects of acetylsalicylic acid and gland weights, white blood cell counts, and prothrombin time of chickens.

METHODS AND PROCEDURES

All birds were from the same strain of New Hampshires developed at the Mississippi State University Agricultural Experiment Station.

In all three trials to be reported, the birds were raised in battery brooders. In the initial trial, eight birds with equal numbers of males and females were placed in each of the top two decks of two separate batteries. During the first wk after hatching, all birds received a basal ration. Two hundred g of acetylsalicylic acid was added to 75 lb of feed (0.58 percent) and fed to the birds in deck one of battery one and deck two of battery two from the first to the fifth wk of age. The basal ration, lacking acetysalicylic acid, was administered to the birds in the two remaining decks. Therefore, all treatments were replicated two times. Body weights were recorded weekly; total and differential white blood cell counts were made at one and five wk of age. The Natt-Herrick technique (1946) was employed for the total count and Wright's stain for the differential count. At five wk of age, all the birds were sacrificed and the bursa of Fabricius and adrenals weighed. In a second trial, the effect of reducing the amount of acetylsalicylic acid to 0.07 and 0.15 percent was determined on body weight gains, feed consumption, and prothrombin times during a two-wk period. The procedure of Frost et al. (1956) was followed for the determination of prothrombin time. The top three decks of three batteries were used. Each treatment was assigned a different deck in each of the three batteries. In the final trial, the response of body weight, gland weights, and white blood cell counts to intramuscular injections of a saline solution of sodium salicylate was studied. The experimental design was the same as in trial two. Six bursae from each group were saved, sectioned, and stained with haemotoxylin and eosin. The white blood cell counts and body weight data were analysed by the analysis of variance while the gland weights were analysed by the analysis of covariance (Snedecor, 1946). Significant treatment differences were determined by Duncan's new multiple range test (1955). Means (tables 1 through 5) are accompanied by their standard deviations.

RESULTS AND DISCUSSION

Cortisone acetate, a glucocorticoid, will (1) decrease the growth rate of young birds (Glick, 1957), (2) decrease the size of the bursa of Fabricius (Glick, 1957, 1959) (Huble, 1958), and (3) increase the number of circulating heterophils

(Bannister, 1951) (Huble, 1955) (Glick, 1958). Also, stressor agents which appear to stimulate glucocorticoid production by stimulating ACTH release will cause regression of the bursa (Garren and Shaffner, 1956) and an increase in heterophil counts (Newcomer, 1958). Therefore, the reduced body weight in the presence of acetylsalicylic acid (table 1) cannot adequately be explained on the basis of an increased output of glucocorticoids since the bursa of Fabricius did not regress and the heterophil counts did not increase.

The growth suppressing effect of acetysalicylic acid was not apparent when the drug was reduced to the 0.07 and 0.15 percent level (table 3). Also, acetylsalicylic acid did not exhibit a hypoprothrombinemic action.

TABLE 1

The influence of feeding acetylsalicylic acid (0.58%) from the first to fifth week of age on body weight, and weight of the bursa of Fabricius and adrenal glands of New Hampshire chicks

	Treatments[1]	
	Basal	Acetylsalicylic acid
Body weight, g		
Initial (1 wk of age)	55	54*
Final (5 wk of age)	457	419
Bursa of Fabricius, g	1.7378±.55	1.510±.72
Adrenals, mg	67.7±1	59.3±9

[1]Each mean includes 16 birds.
*All means not underscored by the same line are significantly different (Duncan, 1955).

TABLE 2

The influence of feeding acetylsalicylic acid (0.58%) from the first to fifth week of age on the white blood cell count of New Hampshire chicks[1]

	Treatments*	
	Basal	Acetylsalicylic acid
Total white blood cells, cells/mm³ x 1000		
Initial (1 wk of age)	9.2±2	10.4±4
Final (5 wk of age)	13±3	14.5±4
Lymphocytes, %		
Initial	91±3	91±3
Final	92±2	92±3
Heterophil, %		
Initial	6±3	6±2
Final	5±1	5±2

[1]Each mean includes 16 birds.
*No significant mean differences existed.

The intramuscular injection of 16 mg of sodium salicylate per 100 g of body weight (table 4) significantly reduced body weight gains, but did not significantly affect the weights of the bursa of Fabricius and adrenal glands. All the bursae, with the exception of one from the saline and salicylate groups, histologically exhibited lymph follicles with a single layer of epithelial cells separating the cortex and medulla of the follicle and many lymphoid cells in the medulla. This histological picture is one commonly observed during bursa growth and prior to bursa involution. The remaining two bursae exhibited an obvious hyperplasia of

TABLE 3

The effect of feeding acetylsalicylic acid on body weight gains, feed consumption, and prothrombin times of 18-day-old New Hampshire chicks

	Treatments*		
		Acetylsalicylic acid	
	Basal	.15%	.07%
Gain in body weight, g, 90 birds/treatment			
4 to 11 days of age	62	60	57
11 to 18 days of age	92	94	87
Feed consumption/bird, g	385	381	373
Prothrombin time, sec, 16 birds/treatment	26.7±5	28.1±2	28.3±3

*No significant mean differences existed.

TABLE 4

The effect of seven consecutive injections of sodium salicylate on gain in body weight and gland weights of 6-week-old New Hampshires

	Treatments*		
	CONTROL, no injection	Saline, 0.2 cc/injec.	Sodium salicylate[1], 0.2 cc/injec.
Gain in body weight, g 21 birds/treatment	122±19	122±18	98±39
Bursa of Fabricius, mg/100 g of body weight	366.1±80.7	340.9±85.6	336.5±94.4
15 birds/treatment			
Adrenals, mg/100 g of body weight	10.5±1.0	10.9±2.0	10.9±.1
15 birds/treatment			

[1]Each injection equivalent to 100 mg of sodium salicylate; approximately 14 to 16 mg of sodium salicylate/100 g of body weight.

*All means not underlined by the same line are significantly different at the 1% level, Duncan (1955).

epithelial cells separating the cortex and medulla of the follicle as well as a decline in the lymphoid cells of the medulla and an increase in the epithelial cells of this region. This histological picture is characteristic of bursa involution. The bursae weight of these two birds was one-half of the mean for their group. The salicylate injections did not significantly affect the white blood cell counts (table 5). Again, the salicylate's depressing action on body weight cannot be explained on the basis of an increased release of glucocorticoids which are catabolic to growth rate or on reduced feed consumption which was approximately equal between the groups.

According to Cochran (1952), salicylates produced a marked and progressive increase in the oxygen consumption of man. This suggested that the salicylates may have interfered with the oxidative phosphorylating reaction (Smith, 1954). The growth suppressing effect of acetylsalicylic acid and sodium salicylate of this experiment may have resulted from an inhibition of high-energy-phosphate bonds. A reduced production of high-energy-phosphate bonds would, according to Smith

TABLE 5

The influence of seven consecutive injections of sodium salicylate on the white blood cell count of 6-week-old New Hampshires

	Treatments*		
	Control, no injection	Saline, 0.2 cc/inj.	Sodium salicylate, 0.2 cc/injection 100 mg salic./inj.
Total white blood cells, cells/mm³ x 1000			
4 hr after 1st inj.	25.6±9	22.4±5	26.7±9
12 hr after 7th inj.	25.4±9	24.0±5	17.2±3
Lymphocytes, %[1]			
4 hr after 1st inj.	86±7	88±10	77±9
12 hr after 7th inj.	85±8	85±9	87±4
Heterophil, %[2]			
4 hr after 1st inj.	10±6	9±9	20±7
12 hr after 7th inj.	12±7	13±8	11±5

[1]The absolute number of lymphocytes of the sodium salicylate birds was 1,400 and 6,900 cells/mm³ lower than the control counts in the 4 and 12 hr groups, respectively.

[2]The absolute number of heterophils of the sodium salicylate birds was 3,800 and 1,300 cells/mm³ higher and lower than the counts in the 4 and 12 hr groups, respectively.

*All means based on 8 birds.

(1954), result in the sacrifice of increasing amounts of substrate to supply the energy required for the phosphorylating processes.

SUMMARY

The effects of oral administration of acetylsalicylic acid and intramuscular injections of sodium salicylate on body weight, weights of the bursa of Fabricius and adrenal glands, prothrombin time, and white blood cell counts of young birds were studied. High levels of acetylsalicylic acid (0.58 percent) depressed body weight, but had no influence on gland weights or white blood cell counts. Low levels of acetylsalicylic acid (0.07 and 0.15 percent) did not affect body weight or prothrombin time. Intramuscular injections of sodium salicylate significantly reduced body weight gains, but had no significant influence on gland weights or white blood cell counts. The data indicate that acetylsalicylic acid or sodium

salicylate at the levels administered do not stimulate the pituitary-adrenal axis of young chickens.

REFERENCES

Bannister, G. L. 1951. Avian blood changes following injections of cortisone. Canadian J. Comp. Med. 15: 169–171.

Barnett, G. O., and **R. S. Teague.** 1958. The antagonism of salicylates to diethylstilbestrol upon liver glycogen in the rat. Endocrinology 63: 205–211.

Clark, B. B., and **M. Spitalny.** 1946. Prothrombinopenic activity of the salicylates and pharmacologically related drugs. Fed. Am. Soc. Exptl. Biol. 5: 171.

Cochran, J. B. 1952. The respiratory effects of salicylate. British Med. J. 2: 964–967.

Cronheim, G., J. S. King, Jr., and **H. Hyder.** 1952. Effect of salicylic acid and similar compounds on the adrenal-pituitary system. Proc. Soc. Exptl. Biol. and Med. 80: 51–55.

Duncan, D. B. 1955. Multiple range and multiple F test. Biometrics 11: 1–42.

Field, J. B. 1945. Hypoprothrombinemia induced in suckling rats by feeding 3,3′-methylene-bis(4-hydroxycoumarin) and acetylsalicylic acid to their mothers. Am. J. Physiol. 143: 228–242.

Frost, D. V., H. S. Perdue, and **H. C. Spruth.** 1956. Vitamin K activity of menadione sodium bisulfite in chickens. J. Nutrition 59: 181–197.

Gaebler, O. H., R. Glovinsky, H. Lees, and **T. Vitti.** 1957. Certain metabolic effects of corticotropin, hydrocortisone, prednisone, and aspirin in normal dogs. Canadian J. Biochem. and Physiol. 35: 1183–1188.

Garren, H., and **C. S. Shaffner.** 1956. How the period of exposure to different stress stimuli affects the endocrine and lymphatic gland weights of the young chicken. Poultry Sci. 35: 266–272.

Glick, Bruce. 1957. Experimental modification of the growth of the bursa of Fabricius. Poultry Sci. 36: 18–23.

———. 1958. The effects of cortisone acetate on the leukocytes of young chickens. Poultry Sci. 37: 1446–1452.

———. 1959. Experimental production of the stress picture with cortisone and the effect of penicillin in the young chicken. Ohio J. Sci. 59: 81–86.

Gross, M., and **L. A. Greenberg.** 1958. The Salicylates. Hillhouse Press, New Haven, Conn. pp. 380.

Huble, J. 1955. Haematological changes in cockerels after ACTH and cortisone-acetate treatments. Poultry Sci. 34: 1357–1360.

———. 1955. Effects of hormones on endocrine and lymphoepithelial glands in young fowl. Poultry Sci. 37: 297–301.

Krantz, J. C., K. Iwamoto, and **de C. B. Farson.** 1946. A contribution to the pharmacodynamics and therapeutics of acetyl-5-bromosalicylic acid. Anesthesia & Analgesia 25: 221–226.

Natt, M. R., and **C. A. Herrick.** 1946. A new blood diluent for counting the erythrocytes and leukocytes of the chicken. Poultry Sci. 31: 735–738.

Newcomer, W. S. 1958. Physiological factors which influence acidophilia induced by stressors in the chicken. Am. J. Physiol. 194: 251–254.

Smith, M. J. H. 1954. Effect of salicylate on liver glycogen in the rat. Biochem. J. 57: 349–353.

Snedecor, G. W. 1946. Statistical Methods. Iowa State College Press, Ames, Iowa. pp. 485.